UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,857	03/08/2005	Claudio Soto	2641-1-001PCT/US	3342

23565 7590 06/11/2007

KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
06/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,857	SOTO ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006 and 05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-11,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-19* is/are rejected.

7)☒ Claim(s) *12,13,15,17 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed November 27, 2006 in response to the Office Action of May 22, 2006 is acknowledged. The species election filed March 5, 2007 is acknowledged. Applicant elected with traverse Group III, claims 12-14 and 17-19 and the species SEQ ID NO:2.

2. Applicants argue that the Groups designated by Examiner fail to define compositions and methods with properties so distinct as to warrant separate examination and search. Applicants argue that a search of any of the methods separately classified by Examiner as the invention of Group III would require an additional search of the identical classes wherein the methods of Groups IV are classified this resulting in a duplicate search of the same material (p. 3).

The arguments have been considered and are found partially persuasive with respect to rejoining Group IV with Group II for examination. All other Groups, however, remain restricted for the reasons set forth in the previous Office Action (p. 3-4): "The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-V appears to be an apoptogenic-bacteriocin capable of inducing apoptosis in malignant cells.

However, said technical feature does not constitute a special technical feature in view of Farkas-Himsley et al I, Cell Mol Biol, 1992, 38:643-651. Farkas-Himsley et al I teach bacteriocin that selectively kills malignant cells by inducing apoptosis (abstract).

Therefore, the technical feature linking the inventions of Groups I-V does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art. Accordingly, Groups I-V are not so linked by the same or a corresponding special technical feature as to form a single general incentive concept and restriction for examination purposes as indicated is proper."

Thus, the "special technical feature" does not define a contribution over the prior art. For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL

3. Group IV is rejoined with Group III for examination purposes. Claims 1-21 are pending. Claims 1-11, 20, and 21 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 12-19 as drawn to SEQ ID NO:2 are currently under prosecution.

Claim Objections

4. Claims 12, 13, 15, 17, and 18 are objected to for containing subject material that is drawn to a non-elected invention. The claims recite "apoptogenic-bacteriocin **of Claim 1**" which is a non-elected claim. Amendments of the claims to include all of the

limitations of claim 1 and to delete referenced claim 1 would obviate the rejection.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 14, 16, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to a method comprising administering an apoptogenic-bacteriocin comprising the amino acid sequence of SEQ ID NO:2 or **an active portion or analog thereof.**

The specification discloses SEQ ID NO: 2 for the processed, active microcin E492 (p. 4, section 010; p. 10, section 030; Figure 7). The specification does not disclose any other active portions or analogs of SEQ ID NO:2 as broadly encompassed in the claims.

The art (see Lagos et al, J of Bacteriology, 1999, 181:212-217; Figure 1) teaches the sequence of microcin E492 (see sequence search "20070524_13305_us-10-506-

857-2.rup", Result # 1, UniProt database), however the sequence of microcin E492 does not provide and adequate representative number of species to support adequate written description for the broad genus of an active portion or analog of SEQ ID NO:2 as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "an active portion or analog thereof". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical

properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of active portions or analogs thereof, per Lilly by structurally describing representative active portions or analogs for SEQ ID NO:2 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe active portions or analogs thereof useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses SEQ ID NO:2 as the processed, active microcin E492, this does not provide a description of the broadly claimed active portions or analogs thereof that would satisfy the standard set out in

Enzo because the specification provides no functional characteristics coupled to structural features.

Further, the specification also fails to describe active portions or analogs thereof for SEQ ID NO:2 by the test set out in Lilly because the specification describes only SEQ ID NO:2 for E492. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of a active portions or analogs thereof that is required to practice the claimed invention. Since the specification fails to adequately describe the product to which the claimed method uses, it also fails to adequately describe the method.

6. Claims 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed

invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for the treatment or **prevention of cancer in a mammal** comprising administering to said mammal apoptogenic-bacteriocin of claim 1 or comprising the amino acid sequence of SEQ ID NO:2 or an active protein or analog thereof (claims 17-19).

The specification discloses that active microcin E492 (SEQ ID NO:2) was administered to HeLa cells *in vitro* and induced cell death via apoptosis (Example 6, p. 50). The specification discloses that microcin E492 functions as an apoptogenic-bacteriocin (p. 4, section 010).

The art teaches that microcin E492 is able to kill some human cell lines *in vitro* but not others. Hetz et al (PNAS, 2002, 99:2696-2701) teach that microcin E492 was administered to these cells *in vitro*: HeLa (an epithelial cell line derived from human cervix carcinoma, KG-1 (monocyte-macrophage cell line), RJ2.25 (variant of the Raji B-LCL), Jurkat (a T-cell derived from acute T-cell leukemia), Ramos (a B-cell line

originated from Burkitt's lymphoma, and AMG-3 (human endothelial cells from human tonsils) (p. 2697, col. 1). Cell lines KG-1 and AMG-3 were *insensitive* to microcin E492, all other cell lines were sensitive, at different degrees, to the microcin E492 toxic effect (p. 2698, col. 2; Table 1).

The art further teaches that there is a Partially Purified Bacteriocin (PPB) or verotoxin 1 (VT1) that has anti-cancer activity *in vitro* and *in vivo*, selectively kills malignant cells, and that induces apoptosis in cells (see Farkas-Himsley et al I, 1992, Cellular and Molecular Biology, 38:643-651; see Farkas-Himsley et al II, 1995, PNAS, 92:6996-7000; see US Patent 5,968,894, Lingwood et al, issued 10/19/1999).

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide examples or guidance for the **prevention of cancer in a mammal** comprising administering an effective amount of an apoptogenic-bacteriocin of claim 1 or comprising the sequence of SEQ ID NO:2, an active portion or analog thereof. The specification lacks the critical steps necessary in presenting some type of predictable response in a population of hosts deemed necessary to prevent cancer. Reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer or have had cancer. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and link those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of

the prevention of the disease is the essence of a valid preventive agent. All of this underscores the criticality of providing workable examples which are not disclosed in the specification. Further, the art demonstrates the lack of cancer prevention by an apoptogenic-bacteriocin. Farkas-Himsley et al II (above) teach the administration of a bacteriocin, VT1, to mice *in vivo*, however, tumor growth was not prevented (Table 1).

Therefore, in view of the novel nature of the invention, the state of the art, the lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

7. Claims 12-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **a method for apoptosis of tumor cell or cancer cells in a mammal, the treatment of cancer in a mammal, and reducing cancer growth in a mammal, comprising administering to said mammal an effective amount of the apoptogenic-bacteriocin of claim 1 or comprising the amino acid sequence of SEQ ID NO:2**, does not reasonably provide enablement for a method for apoptosis of *cells undergoing aberrant growth* in a mammal and a method for reducing *any eukaryotic cell growth* or *blocking eukaryotic growth*, comprising administering the said mammal an effective amount of the apoptogenic-bacteriocin of claim 1 or comprising the amino acid sequence of SEQ ID NO:2; and does not reasonably provide enablement for a method for apoptosis of tumor cell or cancer cells,

reducing eukaryotic growth, or treating cancer in a mammal comprising administering any *active portions or analogs of an apoptogenic-bacteriocin comprising SEQ ID NO:2.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to a method for apoptosis of tumor cell, cancer cells, **or cells undergoing aberrant growth** in a mammal comprising administering to said mammal an effective amount of the apoptogenic-bacteriocin of claim 1 or comprising the amino acid sequence of SEQ ID NO:2, or **an active portion or analog thereof** (claims 12-14); a method for a method for **reducing or blocking eukaryotic cell growth in a mammal** comprising administering an effective amount of the apoptogenic-bacteriocin of claim 1 or comprising the sequence of SEQ ID NO:2 or **an active portion or analog thereof** (claims 15 and 16), a method for the treatment of cancer in a mammal comprising administering an effective amount of an apoptogenic-bacteriocin comprising the amino acid sequence of SEQ ID NO:2, or **an active portion or analog thereof** (claim 19).

The specification discloses that active microcin E492 (SEQ ID NO:2) was administered to HeLa cells *in vitro* and induced cell death via apoptosis (Example 6, p. 50). The specification discloses that microcin E492 functions as an apoptogenic-bacteriocin (p. 4, section 010). The specification discloses aberrant cell growth includes but is not limited to benign and malignant tumors, cancers, hyperplasia, tissue hypertrophies, psoriasis and polyps (p. 7, section 021).

The art teaches that microcin E492 is able to kill some human cell lines *in vitro* but not others. Hetz et al (PNAS, 2002, 99:2696-2701) teach that microcin E492 was administered to these cells *in vitro*: HeLa (an epithelial cell line derived from human cervix carcinoma, KG-1 (monocyte-macrophage cell line), RJ2.25 (variant of the Raji B-LCL), Jurkat (a T-cell derived from acute T-cell leukemia), Ramos (a B-cell line originated from Burkitt's lymphoma, and AMG-3 (human endothelial cells from human tonsils) (p. 2697, col. 1). Cell lines KG-1 and AMG-3 were *insensitive* to microcin E492, all other cell lines were sensitive, at different degrees, to the microcin E492 toxic effect (p. 2698, col. 2; Table 1).

The art further teaches that there is a Partially Purified Bacteriocin (PPB) or verotoxin 1 (VT1) that has anti-cancer activity *in vitro* and *in vivo*, selectively kills malignant cells, and that induces apoptosis in cells (see Farkas-Himsley et al I, 1992, Cellular and Molecular Biology, 38:643-651; see Farkas-Himsley et al II, 1995, PNAS, 92:6996-7000; see US Patent 5,968,894, Lingwood et al, issued 10/19/1999).

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide examples or guidance for apoptosis in ***any* cells undergoing any aberrant growth** in a mammal. The specification discloses *in vitro* examples of inducing apoptosis in HeLa cells (cancerous cell line). The art teaches the induction of apoptosis in various cancerous human cell lines comprising administering microcin E492, none of which cell lines are representative of hyperplasia, hypertrophies, benign tumors, psoriasis or polyps *in vitro* or *in vivo* as broadly encompassed by the claims (see Hetz et al). Farkas-Himsley et al I, Farkas-

Himsley et al II, and US Patent 5,968,894 (all above) teach the selective killing of malignant cells *in vitro* and *in vivo* after administration of VT1, however, none of the cell lines or xenografts used are representative of hyperplasia, hypertrophies, benign tumors, psoriasis or polyps as broadly encompassed by the term "cells undergoing aberrant growth". Neither the art nor the specification provide a nexus between the induction of apoptosis in *any* cells undergoing aberrant growth, other than cancerous cells, and the administration of an apoptogenic-bacteriocin of claim 1 or comprising the amino acid sequence of SEQ ID NO:2, or an active portion or analog thereof.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide examples or guidance for **reducing *any* eukaryotic cell growth** in a mammal. The specification and the art (Hetz et al, Farkas-Himsley et al I, Farkas-Himsley et al II, and US Patent 5,968,894 (all above)) teach a reduction in *cancerous* cell growth. Further, Farkas-Himsley et al I, teach the selective killing of malignant cells using an apoptogenic-bacteriocin (abstract) and Hetz et al teach that administration of microcin E492 *in vitro* did not affect the growth of two normal human cell lines that would be considered eukaryotic cells. Given the art teaches the *inability* of two bacteriocins to kill any and all types of eukaryotic cells, one of skill in the art could not predictably reduce any and all eukaryotic cell growth as broadly encompassed by the claims.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide examples or guidance for **blocking eukaryotic cell growth in a mammal.** Farkas-Himsley et al II (above) teach that the

administration of apoptogenic-bacteriocin VT1 *in vivo* wherein tumor growth was NOT blocked (see rejection in section 6 above with regards to "prevention" of cancer). Neither the specification nor the art teach or enable the blocking of any eukaryotic cell growth comprising administering any apoptogenic-bacteriocin.

Finally, one cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide examples or guidance for apoptosis of tumor cells or cancer cells, treating cancer or reducing cancer growth comprising administering any **unknown active portions or analogs** of an apoptogenic-bacteriocin comprising SEQ ID NO:2. Again, the specification has not disclosed the required or conserved structure of any active portions or analogs required to function for inducing apoptosis. The specification and the art (Hetz et al above) teach the induction of apoptosis in cancerous cell lines comprising administering microcin E492 (SEQ ID NO:1 or 2), however, no active portion or analog is disclosed that would predictably function to induce apoptosis as claimed, hence one of skill in the art would not know how to make the claimed active portion or analog that would predictably function to induce apoptosis as claimed.

Therefore, in view of the state of the art, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 12, 15, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,968,894, Lingwood et al, filed 11/28/1995, issued 10/19/1999, and as evidenced by Farkas-Himsley II (1995, PNAS, 92:6996-7000).

The claims are drawn to a method for apoptosis of tumor cells, cancer cells or cells undergoing aberrant growth in a mammal, a method for reducing eukaryotic cell growth in a mammal, and a method for the treatment of cancer in a mammal, comprising administering to said mammal an amount of apoptogenic-bacterium of claim 1.

Lingwood et al teach the administration of verotoxin 1 (VT1) to mammals for the treatment of cancer (abstract; col. 1, lines 15-25; col. 5, lines 12-32; claims 1-12). VT1 has anti-proliferative effects, reduces tumor growth, and induces apoptosis in malignant cells (col. 21, lines 44-54).

As evidenced by Farkas-Himsley II, VT1 is the active component of bacteriocin isolated from a strain of *E. Coli* (HSC_{10}) (abstract).

All the limitations of the claims are met.

9. Claims 12, 13, 15, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hill et al (Cancer Research, 1991, 51:1359-1365), as evidence by Farkas-Himsley et al I (1992, Cellular and Molecular Biology, 38:643-651).

The claims are drawn to a method for apoptosis of tumor cells, cancer cells or cells undergoing aberrant growth in a mammal, a method for reducing eukaryotic cell growth in a mammal, and a method for the treatment of cancer in a mammal, comprising administering to said mammal an amount of apoptogenic-bacterium of claim 1; and a method for apoptosis of tumor cells, cancer cells or cells undergoing aberrant growth or the treatment of cancer in a mammal comprising administering an amount of apoptogenic-bacterium of claim 1 in combination with an anti-tumor or anti-cancer agent or compound.

Hill et al teach a method of treating cancer and reducing tumor growth comprising administering a bacteriocin, Partially Purified Bacteriocin (PPB), to mice injected with KHT sarcoma cells (Fig. 3, Table 1; p. 1363, col. 2; abstract). Hill et al teach administering PPB in combination with cyclophosphamide (CY), a known anti-cancer agent (p. 1360, col. 2 through p. 1361, col. 2; Table 1).

Although Hill et al does not specifically teach that PPB induced apoptosis, as evidenced by Farkas-Himsley et al I, PPB induces apoptosis and selectively kills malignant cells (abstract).

All the limitations of the claims are met.

10. **Conclusion:** No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642